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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SEHARASEYON, JEGATHEESAN	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 07/12/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/747,383	VLASSELAER ET AL.	
	Examiner	Art Unit	
	Jegatheesan Seharaseyon, Ph.D	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 April 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16-23 and 25-28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-23 and 25-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. This office action is in response to the amendment and remarks filed on 4/19/06. Claims 16 and 22 have been amended. Therefore, claims 16-23 and 25-28 are currently pending and are examined.

2. The text of those sections of Title 35, U. S. Code not included in this action can be found in a prior Office action.

3. Any objection or rejection of record, which is not expressly repeated in this action, has been overcome by Applicant's response and withdrawn.

Claim Rejections - 35 USC § 103, maintained

4. The rejection of claims 16-23 and 25-28 under 35 USC 103(a) as being unpatentable over Huland et al. in view of both Debs et al. and Ruskewicz et al. further evidenced by Nayar et al or Hora et al. is maintained for reasons stated in the previous Office Action dated 1/13/03, 11/17/03, 10/29/04, 6/29/05 and 12/29/05. Applicants' arguments have been fully considered but are deemed not to be persuasive. Applicants contend that claim 22 as amended is not taught by the references. Specifically, Applicants contend that Ruskewicz reference does not teach or suggest the claimed particle size range of: (i) less than 1 micron, (ii) 1-3 microns, (iii) 3-5 microns, (iv) 5-10 microns, or (v) greater than 10 microns. However, Ruskewicz reference as acknowledged by the Applicants in their response dated 10/6/05 page 4 does teach "an aerosol preferably having a particle size in the range of about 1 to 12 microns, more preferably of about 3.0 to 6.0 microns." In addition, Ruskewicz reference also teaches aerosol particles that are in the size range of about 0.5 to 12 microns (column 17,

lines34-36). Furthermore, the reference also teaches that a compound can be directed to a particular area of the lung which needs treatment by adjusting the aerosol particles size (column 17, lines 38-40). See MPEP § 2144.05 [R-3] for case law pertaining to rejections based on the overlap of ranges. "In the case where the claimed ranges "overlap or lie inside ranges disclosed by the prior art" a prima facie case of obviousness exists. *In re Wertheim*, 541 F.2d 257, 191 USPQ 90 (CCPA 1976); In re Woodruff, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990) (The prior art taught carbon monoxide concentrations of "about 1-5%" while the claim was limited to "more than 5%." The court held that "about 1-5%" allowed for concentrations slightly above 5% thus the ranges overlapped.)" With respect to Applicants arguments regarding examiner using hind sight reasoning (page 5 of the response), it is not found to be persuasive because both 3-5 microns and 5-10 microns overlap with referenced 3-6 microns. Therefore, absent evidence to the contrary particle sizes of less than 1 micron, 1-3 microns, 3-5 microns, 5-10 microns and greater than 10 microns are all obvious over the prior art. Thus contrary to Applicants assertion references in combination make the instant invention obvious over prior art.

Applicants again assert that the cited references does not teach or suggest claimed retention of "substantially the same biological activity". The Office discussed extensively in the Office Action dated 10/29/04 on page 3 that "Debs et al. reference teaches the use of aerosolized IFN-gamma to stimulate alveolar macrophage and blood monocyte function (abstract). It also discusses that IFN-gamma activates macrophages to release IL-1, express class II HLA (Ia) surface Ag, and lyse tumor cells. Therefore,

clearly demonstrating that the IFN-gamma biological activity in the aerosol composition contains substantially the same biological activity as that of the solution. In addition, Debs et al. provide an analysis of rHuTNF- α recovered as a condensate after aerosolization demonstrated that it retained full biological activity, as indicated by migration non-denaturing gels (page 3487, 3rd paragraph) and by the ability to growth inhibit tumor cell *in vitro*. Therefore, absent evidence to the contrary it is assumed that the cytokine activity of the aerosol compositions is substantially the same as that of solution. Further, it should be noted that, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986)." Though the Applicants contend that that the Debs reference does not measure the biological activity of γ-IFN, as discussed above it does teach measuring of rHuTNF- α (also a member of the cytokine family and a multimeric protein) biological activity to demonstrate that it contains the full biological activity after aerosolization (page 3487, 3rd paragraph). Thus, absent evidence to the contrary it would be expected that this biological activity of interferon gamma to be substantially same to the aqueous solution (as discussed above aerosolized IFN-gamma activates macrophages to release IL-1, express class II HLA (Ia) surface Ag, and lyse tumor cells).

With reference Applicants assertion that the cited references does not teach or suggest claimed retention of substantially the same molecular size distribution, the Office previously discussed extensively in the Office Action dated 11/17/03 on pages 3-

4 the molecular size distribution. Again, Ruskewicz et al. teach that the size of the particles be in the range 0.5 to 12 microns, mean particle size be within a narrow range, so that 80% or more of the particles being delivered to the patient (limitation of new claim 22) have a particle diameter that is within ± 20% of the average particle size, preferably within ± 10%, and more preferably within ± 5% of the average particle size of the drug (column 17, lines 45-50). **Thus, meeting the limitation of γ-IFN molecular size distribution substantially the same as that aqueous solution.** It is noted that particles within ± 5% of the average is considered within two standard deviations of the mean. This also meets the limitation recited in claim 23, wherein at least 95% of the droplets have a size in the selected size range. Furthermore, Applicant discusses limitations not present in the instant claims with respect to dimerization or aggregation of gamma-interferon and its effect on aerosolization. Therefore, rejection of claims 16-23 and 25-28 (newly added) under 35 U.S.C. 103(a) as being unpatentable over Huland et al. (U. S. Patent No. 5,780,012) in view of both Debs et al. (J.of Imm. Vol. 140: 3482-3488) and Ruskewicz et al. (U. S. Patent No. 5,971,951) is maintained.

5. The rejection of claims 16-23 and 25-28 under 35 USC 103(a) as being unpatentable over Huland et al. and Jaffe et al. in view of both Debs et al. and Ruskewicz et al. further evidenced by Nayar et al or Hora et al. is maintained for reasons stated in the previous Office Action dated 10/29/04, 6/29/05 and 12/29/05. Applicants' arguments have been fully considered but are deemed not to be persuasive. Applicants' traverse the rejection essentially for the same reasons as stated above in

paragraph 4. Thus, the rejection is maintained for reasons stated previously and above in paragraph 4.

Claim Rejections - 35 USC § 112, second paragraph, maintained

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 16-23 and 25-28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6a. The rejection of claim 22 as being vague and indefinite in the recitation of the term "biological activity substantially the same" is maintained. Applicants' arguments have been fully considered but are deemed not to be persuasive. Again as stated previously it is unclear if this means the activity is same or within a range. Specification does not provide any guidance for biological activity that is substantially the same. For example, if the liquid droplet lyses 50% of tumor cells will it considered to be having substantially same biological activity? Claims 16-21, 23 and 25-28 are rejected insofar as they depend on rejected claim 22.

6b. The rejection of claim 22 as being vague and indefinite in the recitation of the term "molecular size distribution substantially the same" is maintained. Applicants' arguments have been fully considered but are deemed not to be persuasive. It is unclear if this means the size is same or within a limited acceptable range. Specification does not provide any guidance for molecular size distribution that is substantially the

same. Applicants have not provided the molecular size distribution of the aqueous interferon gamma solution. Claims 16-21, 23 and 25-28 are rejected insofar as they depend on rejected claim 22.

7. No claims are allowable.

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jegatheesan Seharaseyon, Ph.D whose telephone number is 571-272-0892. The examiner can normally be reached on M-F: 8:30-5:00. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on 571-272-0961. The fax phone

number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JS 7/06

CHRISTINE J. SAOUD
PRIMARY EXAMINER

Christine J. Saoud